IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

THERMO FINNIGAN LLC, Plaintiff and Counterclaim Defendant, v. APPLERA CORPORATION, Defendant and Counterclaim Plaintiff.	Civil Action No. 04-1505-GMS

APPLERA CORPORATION'S ANSWERING CLAIM CONSTRUCTION BRIEF

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Defendant Applera Corporation ("Applera") submits this answering brief in response to the opening claim construction brief of Thermo Finnigan LLC ("Thermo"). (D.I. 57).

SUMMARY OF ARGUMENT

In its recent *en banc* decision on claim construction, the Federal Circuit emphasized that claims should be construed to reflect the actual invention the inventors made. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1321 (Fed. Cir. 2005); *See also Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, No. 05-1373, slip op. at 7-10 (Fed. Cir. February 15, 2005) attached hereto as Exhibit A. The Federal Circuit therefore rejected the use of dictionaries rather than the patent specification as the starting point. *Phillips*, 415 F.3d at 1321. Thermo disregards these admonitions. Instead, Thermo relies heavily—in some cases almost exclusively—on dictionaries as the starting point for its claim construction analyses. Thermo's motivation is clear: the devices that Thermo has accused of infringement do not use the invention the inventors made and described in their patent specification. To succeed, Thermo must redefine the invention to encompass technology its inventors never conceived.

Applera's constructions, in contrast, align the claims with the invention the inventors described in the specification. Applera's constructions are true to the understanding persons skilled in the art would have of the claim terms from reading the specification, exactly as precedent requires. *See id.* at 1313.

ARGUMENT

A. "Anions"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"anions"	11	Low molecular weight monomeric negatively charged ions.	Negatively charged ions.

In *Phillips*, the Federal Circuit stated that "[u]ltimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim." *Id.* at 1316 (citations omitted). Thermo asserts that "the invention of the '654 patent is directed to improved methods for detection and separation of anions *generally*." (D.I. 57 at 13) (emphasis added). Therefore, it argues, the broad dictionary meaning of anions applies. Thermo cites two sentences in the specification for the proposition that the invention embraces all anions. (*Id.*) Neither sentence supports Thermo's position.

The first sentence, which is also the first sentence in the specification, states that "[t]he *present invention* relates to the separation and detection of *common* anionic species using capillary electrophoresis, and more particularly to the use of temperature control in a capillary electrophoresis system to improve separation and reproducibility of *such* ionic species." (JA 12, 1:7-12) (emphasis added). This sentence does not support Thermo's position that the invention concerns "anions generally." Instead, it confirms that the invention applies to "*common* anionic species."

The second sentence Thermo cites, which is the second sentence in the "Summary of the Invention" states that "[b]oth organic and inorganic anions may be separated." (JA 12, 2:24-25). If the invention embraced all anions, as Thermo argues, the specification would not need to point out that both organic and inorganic anions may

be separated. The reason it does so is because much of the "Background of the Invention" section that precedes this sentence discusses the problem of separating and detecting "most inorganic ions" because they do not absorb light, and because some have similar migration rates. (JA 12, 1:38-39; 2:6-10,15-19). Thus, this sentence clarifies that—in addition to "most inorganic ions"—the invention is also directed to organic anions that present the same types of separation and detection difficulties discussed in the "Background" section.

Lacking support in the specification for the proposition that the invention is directed to "anions generally," Thermo resorts to the "dictionary first" methodology the Federal Circuit discredited in *Phillips*. Thermo quotes dictionary definitions and argues that "[t]he specification does not limit the invention to a particular type of anion that is to be detected and separated." (D.I. 57 at 12-13). However, consulting the specification from the perspective of those skilled in the art first, as *Phillips* requires, makes clear that the inventors used the term "anions" to refer exclusively to low molecular weight monomeric negatively charged ions. The specification repeatedly describes the "invention" as relating to "common," "small" and "low molecular weight" anions. (D.I. 60 at 15-17). A person of ordinary skill in the art would thus understand that the invention is not directed to all negatively charged ions, but specifically to low molecular weight monomeric negatively charged ions.

Indeed, a person skilled in the art would understand that it would not be possible to employ the capillary electrophoresis method described in the '654 patent to separate and detect high molecular weight polymeric anions such as DNA. The type of capillary electrophoresis described in the specification of the '654 patent was known as "capillary

zone electrophoresis," "CZE" or "free solution capillary electrophoresis." (JA 12, 1:18-22, 23). These terms were used to describe the electrophoretic separation of analytes in a solvent when "there is no secondary influence – other than the structure of the analyte and the solvent." (Capillary Electrophoresis: Theory and Practice (Grossman and Colburn eds., Academic Press 1992) at 111 (B 16)[1] ("Grossman")). Free solution capillary electrophoresis was ineffective for separating large polymeric anions such as DNA. (Grossman at 114, B 19) ("As it turns out, for many practically important applications, DNA . . . in particular, separations based solely on differences in free-solution electrophoretic mobilities are not possible."). Separations of such larger, polymeric anions required an additional separation mechanism, such as forcing the anions to travel through a porous polymer gel network. The term "capillary gel electrophoresis" was used to describe this mechanism, *i.e.*, the electrophoretic separation of analytes using a polymer gel in the capillary to achieve separation. (Capillary Electrophoresis Guidebook, (K. Altria ed., Humana Press, 1996) at 157 (B 34)). Capillary gel electrophoresis had been employed in the prior art to separate ions of complex biomolecules like oligonucleotides, RNA and DNA. (Grossman at 146-154, B 21-29). As Thermo notes in its brief, the inventors were well aware that capillary gel electrophoresis could be employed to separate high molecular weight anions such as peptides. (D.I. 57 at 15). Yet, the '654 patent contains no mention of capillary gel electrophoresis at all, much less the use of capillary gel electrophoresis to separate and detect higher molecular weight or polymeric anions such as DNA, RNA or the like. The

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[1] "B __" refers to the Appendix to Applera Corporation's Answering Claim Construction Brief.

'654 patent describes only the separation and detection of low molecular weight monomeric negatively charged ions.[2]

Thermo raises two principal objections to Applera's proposed construction. First, it incorrectly contends that Applera's construction confines the term "anions" to a preferred embodiment. (D.I. 57 at 13-14). The invention is directed to separating and detecting low molecular weight monomeric anions, which is not merely a preferred embodiment—it is the *only* embodiment. Thermo incorrectly asserts that

> the specification describes *a preferred embodiment* that is "particularly suited to detect such common low molecular weight inorganic and organic anions such as chloride, nitrate, nitrite, sulfate, and oxalate."

(D.I. 57 at 13-14) (emphasis added). Thermo's quotation of the specification is misleading. The text Thermo conveniently omits, which is found in the "Summary of the Invention" section of the patent, does not discuss merely a preferred embodiment; it discusses *the invention* itself:

> The *present invention* is particularly suited to detect such common low molecular weight inorganic and organic anions such as chloride, nitrate, nitrite, sulfate, and oxalate.

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[2] As Applera stated in its opening Brief, adoption of Thermo's construction of "anions" would make asserted claims claim 11 and 15 invalid under 35 U.S.C. § 112 because the '654 patent does not describe a method for separating and detecting high molecular weight polymeric anions. *See, e.g., Wang v. America Online, Inc.*, 197 F.3d 1377, 1382-83 (Fed. Cir. 1999) (limiting "frame" to "character-based display systems" because the only system "described and enabled in the [patent] specification and drawings uses character-based protocol" and excluding "bit-mapped display systems" because otherwise the claims would be invalid for failure to satisfy 35 U.S.C. § 112); *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473 (Fed. Cir. 1998). (*See also* D.I. 60 at 18-21). Where a construction is supported by the intrinsic evidence and a competing construction will result in the claim being invalid under § 112, the court should adopt the construction that preserves the validity of the claim. *Wang*, 197 F.3d at 1383. For this additional reason, the Court should reject Thermo's proposed construction.

(JA 13, 3:5-8) (emphasis added). Defining the invention in a limited manner in the "Summary of the Invention" section of the patent specification supports a limited definition of the claim term. *See C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 864 (Fed. Cir. 2004); *Terlep v. The Brinkmann Corp.*, 418 F.3d 1379, 1383 (Fed. Cir. 2005); *Genzyme Corp. v. Transkaryotic Therapies, Inc.*, 346 F.3d 1094, 1099 (Fed. Cir. 2003).

Thermo cites *Interactive Gift Express Inc. v. CompuServe, Inc.*, 256 F.3d 1323, 1341 (Fed. Cir. 2001) in support of its position that "anions" should be read more broadly than described in the specification. That case is inapposite. There, the Federal Circuit held that an "authorization code" in a software algorithm did not include a "decoding" function because, among other things, the specification explicitly stated "in the context of the preferred embodiment" that "decoding occurs . . . 'in response to receiving the authorization code.'" *Id.* Thus, the specification clearly distinguished "authorization" from "decoding" as two different steps in a sequence, and, accordingly, the Federal Circuit held that the term "authorization code" was not limited to a code which included a decoding function. *Id.* In contrast, the '654 specification never indicates that "anions" means anything other than low molecular weight anions, and, in particular, never describes low molecular weight anions as a preferred embodiment of the invention. Instead, it defines the invention as a solution to the specific problem of separating and detecting low molecular weight anions.

The facts here are analogous to those in *Genzyme Corp. v. Transkaryotic Therapies, Inc.*, 346 F.3d 1094, 1097-1104 (Fed. Cir. 2003). There, the Federal Circuit upheld the district court's claim construction that "chromosomally integrated" meant "the

combining or bringing together or merging of . . . the chromosome of the host cell and an **exogenous** nucleotide sequence." *Id.* at 1097 (emphasis in original). The patent owner argued that the claims "do not specify the origin of nucleotide sequences to be inserted into a target cell's chromosome." *Id.* at 1098. According to the patent owner, "chromosomally integrated" only required the coding sequence of interest to be "located in the chromosome," and, therefore, it argued that the district court "impermissibly limited the claim to the preferred embodiment." The Federal Circuit rejected that argument, holding that the district court had correctly limited the claims in this manner because

> both the specification and the prosecution history indicate that the patentee employed the term "chromosomally integrated" in a manner inconsistent with a broad textbook meaning that envelopes both endogenous and exogenous sources of sequences encoding genes in a host cell.

Id. at 1104. Likewise, here, the inventors used "anions" more narrowly than its dictionary meaning, and their more narrow meaning should prevail.

Second, apparently anticipating the rejection of its argument that Applera's construction is restricted to the preferred embodiment, Thermo takes the opposite tack and argues that Applera's proposed construction of "anions" excludes a preferred embodiment. (D.I. 57 at 15). Specifically, relying on a definition of "monomeric unit" as meaning something that "is capable of combining to form a polymer," Thermo contends that Applera's construction excludes the preferred embodiments of chloride, nitrate, nitrite, and sulfate because these anions "do not form monomeric units and cannot be incorporated into a polymer as a 'constitutional unit of a polymer.'" (*Id.*) Thermo mischaracterizes Applera's position. Applera does not employ the term "monomeric unit" in its proposed construction and its construction does not require that the identified

anions be capable of incorporation into a polymer. Rather, Applera employs the term "monomeric" to modify "ion." A "monomeric" ion is an ion "relating to, characteristic of, or *resembling* a monomer." (A 13) (emphasis added). All the anions described in the '654 patent are "monomeric" in that they resemble monomers, which are "relatively simple compounds," in contrast to a polymer such as DNA. Thus, Applera's inclusion of the term "monomeric" in its proposed construction does not exclude any embodiment of the '654 patent.

Finally, Thermo points to the Kurosu article, cited in the prosecution history, to support its position that the term "anions" should include "polymeric" ions, such as peptides. (D.I. 57 at 15-16). However, the inventors did not incorporate by reference or even cite the Kurosu article. The examiner cited Kurosu but did not apply it to reject claims. (JA 63). Therefore, the record does not indicate what if any relevance the examiner perceived it to have. Thermo asserts that the examiner's citation of Kurosu shows that "the inventors were aware of capillary electrophoresis techniques used to detect and separate polymeric ions"—a proposition that is both illogical and irrelevant. (D.I. 57 at 15). There is no evidence that the inventors believed the Kurosu article to be even marginally relevant to their invention. Rather, since persons skilled in the art, including the inventors, knew at the time the patent application was filed that capillary gel electrophoresis could be used to separate and detect larger, polymeric anions, such as DNA and RNA, the absence of *any* reference to such anions or to capillary gel electrophoresis to separate and detect such anions leads to only one conclusion: the inventors of the '654 patent did not consider the separation and detection of such anions within the scope of their invention.

B. "Capillary Electrophoresis"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"capillary electrophoresis"	11	A chemistry technique which utilizes the differences in solute electrophoretic velocity to isolate the various components of a sample in a capillary.	Electrophoresis, or the movement of ions under the influence of an electric field, that takes place in a capillary tube.

Thermo proposes a construction of "capillary electrophoresis" based on dictionary definitions, including non-technical dictionary definitions, and ignores an express definition incorporated by reference in the specification of the '654 patent. Thermo's construction is inaccurate and incomplete.

Capillary electrophoresis is not just the movement of ions in a capillary tube under the influence of an electric field. Thermo's construction says nothing about the separation or isolation of the components of the sample—an essential characteristic of the technique and its main objective. Thermo's construction says nothing about what causes the separation or isolation of the components of the sample—the differences in electrophoretic velocity.

In contrast, Applera's construction adheres to the express definition of capillary electrophoresis stated in the prior art '382 patent and incorporated by reference in the '654 patent. (JA 14, 5:1-14). This definition includes the essential concepts missing from Thermo's construction—that capillary electrophoresis is an isolation and separation technique based on differences in the electrophoretic velocity of the sample components. For example, the specification of the '654 patent explains in its "Background" section that

> [c]apillary zone electrophoresis (CZE) is a powerful and efficient method to *separate* small analytes at very low concentration levels *by exploiting the different mobilities of sample components in an electric field.*

(JA 12, 1:18-22) (emphasis added). Likewise, in its brief's background discussion, Thermo states that "[c]apillary electrophoresis is a technique used to separate . . . ions," and the "[t]the speed at which an ion moves . . . depends on a variety of factors such as the ion's charge, size, and shape." (D.I. 57 at 1). Yet, in its proposed construction, Thermo disregards both the specification and its own explanation, proposing instead that capillary electrophoresis be defined as simply "the movement of ions under the influence of an electric field." (D.I. 57 at 16).

Thermo quibbles with Applera's construction because it uses the term "electrophoretic velocity." However, that term is not disputed and can be explained to the jury by the parties' experts. Indeed, the '382 patent makes clear that electrophoretic velocity is simply the speed at which charged particles move in an electric field during electrophoresis. (JA 204, 1:42-50). This Court should not accept Thermo's apparently simpler, but inaccurate construction.

Aside from criticizing Applera's inclusion of the term "electrophoretic velocity," Thermo states no disagreement with Applera's construction, asserting only that the definition in the '382 patent is not incorporated by reference into the '654 patent. (D.I. 57 at 17). Thermo is wrong. The '654 patent incorporates the '382 patent in its entirety:

> Operation of the thermal control for such a capillary electrophoresis system is described by Weinberger et al. in U.S. Patent No. 5,066,382, *the disclosure of which is hereby incorporated by reference.*

(JA 14, 5:10-14) (emphasis added). Thus, the contents of the '382 patent are part of the specification of the '654 patent. *Advanced Display Systems, Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000).

In any event, whether the '382 definition is or is not incorporated into the '654 patent, it is still appropriate to look to the '382 patent's definition of "capillary electrophoresis" in construing that term because that definition reflects how one of ordinary skill in the art would have understood the term at the relevant time. *See Phillips*, 415 F.3d at 1313 (explaining that "the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention"). An express definition of the term in a prior art reference, particularly one in a patent incorporated by reference into the specification, is certainly more compelling than the inaccurate and incomplete construction proposed by Thermo.

C. "Carrier Electrolyte"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"carrier electrolyte"	11	Any electrically conductive fluid medium.	An electrically conductive fluid medium that carries or transports ions.

The parties agree that the inventors expressly defined "carrier electrolyte" to mean "any electrically conductive fluid medium." (JA 12, 2:56-57). However, on the basis of a single non-technical dictionary, Thermo further proposes that a "carrier electrolyte" is one that "carries or transports ions." This additional language improperly changes the express definition of "carrier electrolyte" found in the '654 patent. The'654 patent claims a method of detecting and separating *anions*, not all ions. Thermo admits as much. (*See, e.g.*, D.I. 57 at 12). As such, Thermo's construction that includes ions, i.e., both anions and cations, is overbroad and not supported by the '654 patent.

Moreover, with no apparent technical support, Thermo's construction improperly incorporates functional elements ("carries or transports ions") into an unambiguous structure (the "medium"). *See Ecolab, Inc. v. Envirochem, Inc.*, 264 F.3d 1358, 1367

(Fed. Cir. 2001); *E.I DuPont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1433 (Fed. Cir. 1988). The intrinsic record contains no evidence that "carrier electrolytes" carry or transport ions, and no explanation of what that would mean. Accordingly, Thermo's construction should be rejected and the express definition found in the '654 specification adopted.

D. "Target Temperature"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"target temperature"	11	A preselected temperature of the fluid in the capillary prior to introducing the sample into the capillary and applying an electrical current to the capillary.	A selected temperature.

Thermo's proposed construction of "target temperature" to mean "a selected temperature" merely substitutes "selected" for "target" without giving any meaning to the claim term. Thermo's construction is purposely abstract. It does not identify what is at the "target temperature" or when. Thermo attacks Applera's construction for providing these answers. Specifically, Thermo asserts that by specifying that the target temperature is the temperature of the fluid in the capillary and that the target temperature is preselected, Applera improperly adds limitations to the term. (D.I. 57 at 20). Thermo is wrong. Applera defines the term in a technically accurate manner based directly on the intrinsic evidence. The "target temperature" is not an abstraction (as Thermo's proposed construction suggests), but instead is the preselected temperature of the fluid in the capillary. *See Phillips*, 415 F.3d at 1313 ("We cannot look at the ordinary meaning of the term . . . in a vacuum. Rather, we must look at the ordinary meaning in the context of the written description and the prosecution history.") (citations omitted).

1. Temperature of the Fluid in the Capillary

Thermo appears to argue that the "target temperature" is the temperature of the capillary, but not that of the fluid in the capillary. (D.I. 57 at 20). This argument makes no sense. For example, the temperature of a room is not the temperature of the walls of the room, but the temperature of the air in the room. More importantly, as Thermo acknowledges, claim 11 explicitly refers to "the temperature *in* said capillary" (JA 16, 10:1-2) (emphasis added), and the '654 patent discloses the presence of fluid in the capillary and the importance of controlling the temperature of the fluid in the capillary:

> Using precise control of *the temperature of the fluid in the capillary* column, the migration speed and order of migration of the anions may be controlled to improve the selectivity of the process. Because the viscosity of the electrolyte solution in which the sample ions migrate is influenced by temperature, close temperature control provides a high degree of reproducibility for samples and enables one to track and identify specific anions.

(JA 12, 2:26-35) (emphasis added);

> By proper selection of a target temperature which is different than ambient temperature . . . and closely controlling the temperature *of the fluid in the capillary* . . . these anionic species may be separated and detected.

(JA 13, 3:21-26) (emphasis added). The '654 patent stands, at least in part, on the premise that precise control of the temperature of the fluid in the capillary allows greater selectivity and reproducibility of results. Thermo's argument that "target temperature" applies to something other than the fluid inside the capillary is specious. There can be no real dispute that "target temperature" properly refers to the "temperature of the fluid in the capillary."

2. Preselected Temperature

Thermo asserts that the "target temperature" need not "be selected prior to introducing a sample into the capillary or applying an electrical current to the capillary."

(D.I. 57 at 21). This assertion is at odds with the claim language, the patent specification and the incorporated '382 patent. It is also illogical.

Citing *Interactive Gift Express*, Thermo argues that "it is a well-known principle of claim construction that the steps of a method claim are not ordinarily limited to the order in which they are recited." (D.I. 57 at 20). However, that case also states that a method claim is limited to the recited order of steps "when the method steps implicitly require that they be performed in the order written." *Interactive Gift Express*, 256 F.3d at 1342. To determine whether the steps of a method claim must be performed in the order they are written, a court must (1) examine the claim language describing the claim steps to determine "if, as a matter of logic or grammar, they must be performed in the order written," and, if not, the court must (2) examine whether the rest of the specification "'directly or implicitly'" requires such a construction. *Altiris, Inc. v. Symantec Corp.*, 318 F.3d 1363, 1369-70 (Fed. Cir. 2003) (quoting *Interactive Gift Express*, 256 F.3d at 1342-43).

Here, the claim language itself rebuts Thermo's argument that the steps can be performed in any order. The first step in claim 11 recites "*providing a capillary* filled with carrier electrolyte." Each of the remaining steps is performed with "said capillary," and, thus, the first step must be performed first. The fourth step of "applying an electrical current to said capillary under conditions causing anions in *said sample* to migrate and separate," can only be carried out after the third step, which is "introducing a sample . . . into said capillary." Similarly, the last step of "detecting said anions" while "maintaining the temperature in said capillary to within ±0.5° C. of said target temperature" cannot be carried out prior to the fourth step of applying the electrical current and causing the

anions to migrate and separate. As a matter of logic and grammar, the claim language requires that the first and third through final steps be carried out in the order recited.

Thermo's argument is thus reduced to a single point: that the second step of "heating or cooling said capillary to a target temperature," unlike all of the other steps, can be taken out of order. Thermo is wrong. Selection of the temperature at which electrophoresis will be performed is a central aspect of the invention. The patent states:

> By proper selection of a target temperature which is different from ambient temperature and which may be higher or lower than ambient, and closely controlling the temperature of the fluid in the capillary to within ±0.5° C., . . . these anionic species may be separated and detected at very low concentrations . . . . A preferred target temperature is in the range from about 25° C to 60° C. *At a selected temperature within that range, the speed and order of migration, and thus the selectivity of the separation of the anions may be precisely controlled.*

(JA 13, 3:21-32) (emphasis added). The target temperature is thus a temperature that is selected before electrophoresis is initiated and at which it is to be performed in order to achieve a beneficial outcome. An electrophoresis run is initiated, in the words of the fourth step of claim 11, by "applying an electrical current to said capillary under conditions causing anions in said sample to migrate and separate." Thus, in order for electrophoresis to be conducted at the "target temperature," the "target temperature" must be established in the capillary *before* electrophoresis is initiated. Accordingly, the second step of claim 11 must precede the fourth step. *See e.g.*, *Loral Fairchild Corp. v. Sony Electronics Corp.*, 181 F.3d 1313, 1321 (Fed. Cir. 1999) (holding that the claim language itself indicated that the steps had to be performed in their written order); *Mantech Envtl. Corp. v. Hudson Envtl. Servs., Inc.*, 152 F.3d 1368, 1375-76 (Fed. Cir. 1998) (holding that the steps of the claim had to be performed in their written order because each

subsequent step referenced something logically indicating that the prior step had been performed).

The specification of the '654 patent supports this conclusion. In the "Summary of the Invention," the '654 patent describes as "one aspect of the present invention, a method for detecting and separating anions" in which the steps of the method are performed precisely as recited in claim 11: a capillary is "provided," the capillary is then heated or cooled to a "target temperature," a sample is introduced, and an electrical current is then applied and anions are separated and detected "while maintaining the temperature in the capillary to within ±0.5°C of the target temperature." (JA 2:36-47; 12, 2:40-47). The incorporated '382 patent[3] likewise provides clear instruction that the target temperature is achieved before the sample is introduced and before the current is applied:

> In accordance with the invention, the following steps are used in order to control temperature. First, a voltage start slope is selected at step 340. . . . Second, a set point ambient temperature is selected at step 342 for the capillary temperature as desired. This is done by the conventional method of monitoring the temperature of the air around the capillary tube and allowing sufficient time at step 344 for the heat transfer process to take place until the capillary tube approaches the target temperature and therefore the temperature in the capillary is very close to that of the surrounding air.
>
> In the next step 346, the electrophoresis separation process in the capillary begins by performing a sample injection and beginning the run...

(JA 209, 11:58-12:10; JA 200, Fig. 11). Indeed, the '382 patent states that "[i]t is important to maintain the temperature of the tube at a stable *predetermined* temperature so as to be able to make measurements at a known temperature." (JA 204, 2:40-43) (emphasis added).

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[3] Thermo does not dispute that the '382 patent is incorporated by reference for its description of temperature control. (D.I. 57 at 17).

Accordingly, "target temperature" properly refers to "a preselected temperature of the fluid in the capillary prior to introducing the sample into the capillary and applying an electrical current to the capillary."

E. "Detecting Said Anions by Simultaneously Monitoring Said Sample at Two Different Wavelengths"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"detecting said anions by simultaneously monitoring said sample at two different wavelengths"	11	Detecting the anions in the sample by simultaneously monitoring the absorption of two different wavelengths of light, one of which is not absorbed by the anions.	Detecting the anions by monitoring the sample at two different wavelengths at the same time.

Thermo's proposed construction of the "detecting" limitation is not a construction. Except for explaining that the word "simultaneously" means "at the same time," Thermo merely parrots the claim language. The meaning of "simultaneously," however, is not in dispute. What is in dispute is whether the claims of the '654 patent can be interpreted as broadly as Thermo asserts.

Ignoring Federal Circuit precedent, Thermo proposes a construction that is untethered from the invention the inventors made and described. *Phillips*, 415 F.3d at 1316 ("the interpretation to be given a claim term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim"). Applera's construction, by contrast, derives from the actual invention. Contrary to Thermo's assertion, Applera's construction does not change the meaning of simultaneous monitoring by adding limitations. Instead, Applera's construction explains what monitoring means in the context of this patent. *See, e.g., Invitrogen Corp. v. Clontech Laboratories, Inc.*, 429 F.3d 1052, 1076-79 (Fed. Cir. 2005) (interpreting the claim terms "lacks RNase H activity" and "substantially no RNase H activity" to require

that the "complete absence of RNase H activity . . . must be shown by the gel assay as set forth in the written description of the '608 patent"). Here, with respect to the simultaneous monitoring embodiment of claim 11, the inventors instruct a person of ordinary skill in the art to "monitor" the sample by observing absorption by the sample at two wavelengths, one of which is not absorbed by the anions.

As explained in Applera's opening brief, the "simultaneously monitoring" embodiment is directed to detecting anions that absorb light strongly at one wavelength but not at another, which produces an electropherogram with unique signatures. (D.I. 60 at 27). The '654 patent specification describes the production of these unique signatures as follows:

> We have also found that simultaneous monitoring by the detector at two different wavelengths provides an additional means of identifying the anions of interest. The nitrogen-containing anions may be distinguished from other anions when absorption is simultaneously monitored at both 210 and 254 nm. For nitrate and nitrite, there is strong absorption at 210 nm but not at 254 nm so that a positive peak is observed at the lower wavelength, but not at the upper wavelength. The presence of positive peaks at 210 nm is thus an identifier of a nitrogen-containing anion in a sample. Additionally, the limits of detection are lower at the shorter wavelength for nitrate and nitrite anions (50 ppb at 210 nm). For other anions such as chloride and sulfate, limits of detection are lower at 254 nm (50 ppb). Thus, by simultaneously monitoring the sample at two different wavelengths, sensitivity of the process is enhanced.

(JA 14, 6:26-42). Likewise, during the prosecution of the '654 patent, the applicants distinguished the prior art on the basis that the claim is directed to the detection of absorption of light, and more specifically to an indirect detection system, *i.e.*, one that includes monitoring of absorption at a wavelength not absorbed by the anions. (JA 122).

Thermo attempts to construe the "detecting" limitation of claim 11 broadly enough to encompass detection methods other than absorbance by relying on dependent

claim 12, which, according to Thermo, is "specifically directed to an absorbance-monitoring detection method in which the 'carrier electrolyte contains a light-absorbing co-anion' and the anions are 'detected indirectly using a photometric detector.'" (D.I. 57 at 23). Thermo's attempted reliance on the doctrine of claim differentiation is misplaced. Claim 11 is limited to monitoring by absorption while claim 12 further defines the carrier electrolyte as including a light-absorbing co-anion. Applera's interpretation does not lead to any contradiction between claim 11 and dependent claim 12.

Although it correctly points out that the specification mentions other methods of detection (D.I. 57 at 23, citing JA 12, 2:48-51), Thermo's citation to this disclosure is misleading. Claim 11, which requires "detecting said anions by simultaneously monitoring said sample at two different wavelengths" (JA 16, 9:43-10:1), is directed to a specific embodiment of the invention. (JA 13, 3:41-44 ("In another embodiment of the invention, anions in a sample may be detected by simultaneously monitoring the sample at two different wavelengths with the photodetector.")); (*see also* D.I. 60 at 27-28). The other methods of detection described in column 2, which are cited by Thermo, have nothing to do with the embodiment described in column 3 and claimed in claim 11. For instance, neither a conductivity detector nor a mass spectrometer (mentioned in column 2) detects anions by monitoring wavelengths, as required by claim 11. Thermo's arguments to the contrary should be rejected.

Finally, Thermo argues that "detecting" should include fluorescent detection because the Jones '506 patent, which is cited in the prosecution of the '654 patent, and the Weinberger '382 patent, mention fluorescent detection. (D.I. 57 at 24). Again, the antecedent for the simultaneous monitoring step in the specification is the embodiment

described in column 3 of the specification, which has nothing to do fluorescent detection and does not even mention fluorescent detection or fluorescence.

F. "Maintaining the Temperature in Said Capillary to within ±0.5°C of Said Target Temperature"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"maintaining the temperature in said capillary to within ±0.5°C of said target temperature"	11	Maintaining the temperature throughout the fluid in the capillary to within ± 0.5°C of the target temperature by monitoring electrical resistance in the capillary and maintaining the resistance at a constant level.	Maintaining the temperature in the capillary to within ±0.5°C of the target temperature.

Thermo's proposed construction of the "maintaining" claim term simply replaces the word "said" with the word "the" in the claim language. As such, it fails to provide any guidance or explanation as to what the limitation means. Applera's proposed construction, in contrast, explains where the temperature is maintained ("throughout the fluid"), and further explains how the temperature is maintained (using the necessary steps of "monitoring electrical resistance in the capillary" and "maintaining the resistance at a constant level"). Applera's construction is supported by the intrinsic evidence and should be adopted.

1. Maintaining the Temperature Throughout the Fluid in the Capillary

Thermo incorrectly contends that Applera's addition of the words "throughout the fluid" contradicts the claim language and is not supported by the intrinsic evidence. (D.I. 57 at 25). As discussed above with respect to "target temperature," the '654 patent discloses controlling the temperature of the fluid in the capillary and the importance of closely controlling that temperature. *See supra* at 15. Although it agrees that the specification discloses maintaining the temperature *of the fluid* in the capillary (citing JA

13, 3:23-25), Thermo argues that because claim 11 is directed to maintaining the temperature *in the capillary*, the claim is not directed to maintaining the temperature *of any fluid in the capillary*. (D.I. 57 at 25). This argument makes no sense, particularly because Thermo does not dispute that the only thing in the capillary is fluid.

Thermo also argues that "nothing in the intrinsic evidence suggests that the temperature would have to be maintained at all points *throughout* the fluid (as compared to *in* the fluid)." (D.I. 57 at 25) (emphasis in original). Contrary to Thermo's argument, the '654 patent explicitly discloses the importance of controlling the temperature throughout the fluid in the capillary:

> . . . *the* temperature at which the process is carried out is crucial to the selectivity of the separation of the anions . . . .

(JA 15, 7:27-29) (emphasis added);

> Using precise control of *the temperature of the fluid in the capillary column*, the migration speed and order of migration of the anions may be controlled to improve the selectivity of the process. Because the viscosity of the electrolyte solution in which the sample ions migrate is influenced by temperature, close temperature control provides a high degree of reproducibility for samples and enables one to track and identify specific anions.

(JA 12, 2:26-35) (emphasis added). Likewise, Thermo admits that it is "important to regulate *the temperature of the capillary electrophoresis system* to ensure consistent separations" and that "temperature control benefits both the reproducibility of the process as well as the selectivity of the anion separation." (D.I. 57 at 8, 26) (emphasis added).

All the above passages refer to "the" temperature in the capillary, that is, a single temperature. A person of ordinary skill in the art would understand that to achieve good selectivity and reproducibility, the temperature in the capillary—*i.e.*, throughout the fluid—must be controlled during a run. Otherwise, there would be no control over the

migration speed or the order of migration of the anions, no selectivity, and no reproducibility. Moreover, as discussed below, the only method the inventors describe for "maintaining" the temperature in the capillary is by monitoring and maintaining the electrical resistance—a method wherein one temperature is maintained "throughout the fluid" in the capillary.

2. By Monitoring Electrical Resistance in the Capillary and Maintaining the Resistance at a Constant Level

Thermo's contends that the claim limitation "maintaining the temperature in said capillary to within ±0.5°C of said target temperature" is "clear and requires no construction." (D.I. 57 at 25). Thermo is wrong. The scenario here is not a simple one, for example, of maintaining the temperature in a room to within a cited temperature range. As explained in Applera's opening brief, there was no customary understanding in the field with regard to maintaining the temperature inside a capillary to within ±0.5°C of the target temperature. (D.I. 60 at 30). Thus, it is necessary to consult the specification of the '654 patent to determine what is meant by "maintaining the temperature in the capillary." *See Phillips*, 415 F.3d at 1315 (stating that the specification "is the single best guide to the meaning of a disputed term").

The '654 patent discloses, through the '382 patent, only *one* method for maintaining the temperature in the capillary: by monitoring electrical resistance in the capillary and maintaining the resistance at a constant level. (D.I. 60 at 30, citing JA 206, 5:7-14; JA 207, 7:63-8:9; JA 209, 12:6-34). Monitoring "the electrical resistance of the capillary provides a means of sensing the temperature of the capillary." (JA 209, 11:33-34). The resistance in the capillary translates to the capillary temperature, "so in effect the capillary is used as a thermometer." (JA 209, 11:44-51). Once the resistance in the

capillary is measured, heat is pumped into or out of the medium surrounding the capillary to maintain the electrical resistance in the capillary at a constant level, thereby providing a constant temperature in the capillary. (JA 209, 12:25-34; JA 200, Fig. 11).

A person of ordinary skill in the art, reading the '654 patent (and the incorporated '382 patent), would understand that to "maintain" a temperature in the capillary, it is necessary both to monitor the temperature in the capillary, *i.e.*, measure any change in the temperature, and then to heat or cool the capillary to control the temperature. Therefore, in light of this disclosure, "maintaining" includes monitoring the electrical resistance in the capillary and maintaining the resistance at a constant level. *See e.g.*, *Invitrogen*, 429 F.3d at 1079.

Thermo incorrectly asserts, however, that the '654 patent specification "discloses a way of maintaining the temperature that does not involve monitoring electrical resistance" because "'[t]he temperature of the capillary tube may be controlled by forced air or liquid circulating around the capillary or by placing the capillary between metal radiator plates.'" (D.I. 57 at 26, citing JA 13, 4:59-62). This is a red herring. The disclosure Thermo cites from the '654 patent relates only to how a capillary tube is heated or cooled, but does not teach a person of ordinary skill in the art how to "maintain" the temperature in the capillary. For example, one cannot maintain a speed by simply knowing how to accelerate or decelerate; one must also monitor the speed to determine whether to accelerate or decelerate. Here, without being able to monitor or measure the temperature in the capillary, one cannot "maintain" that temperature. The only disclosure of how to monitor or measure temperature in the capillary is found in the

'382 patent, which discloses monitoring electrical resistance as a way of monitoring temperature.

Thermo argues that this disclosure of thermal control is a preferred embodiment and should not be part of the construction for the "maintaining" limitation. (D.I. 57 at 27). Thermo, however, has not and cannot point to any other disclosure of thermal control because there is none. Contrary to Thermo's arguments, the disclosure is the *only* disclosure of monitoring the temperature in the capillary found the '654 and '382 patents. Because the '654 patent discloses includes only one scheme for temperature control, the claims should be construed to reflect this limited disclosure. *See, e.g.*, *C.R. Bard*, 388 F.3d at 864; *Wang*, 197 F.3d at 1383.

G. "Electroosmotic Flow"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"electroosmotic flow"	15	The bulk flow of liquid due to the effect of an electric field on cations adjacent to anionic groups immobilized on the capillary wall.	Flow in a capillary under the influence of an electric field.

Thermo's erroneous construction of the term "electroosmotic flow" stems from its reliance on non-technical dictionaries. The general usage dictionary definitions on which Thermo relies make no sense in the context of the '654 patent. (D.I. 57 at 28). For example, Thermo relies on definitions of "electroosmosis" including "the movement of a liquid out of or though a porous material or biological membrane" and "the movement of a conducting liquid . . . through a porous diaphragm." (*Id.*). There is, however, no "porous membrane" or "diaphragm" at issue here. Thus, Thermo's extrinsic evidence is inapposite.

The obvious inapplicability of Thermo's dictionary definitions illustrates why the Federal Circuit has warned against reliance on general dictionary definitions:

> The main problem with elevating the dictionary to such prominence is that it focuses the inquiry on the abstract meaning of words rather than on the meaning of claim terms within the context of the patent . . . . [H]eavy reliance on the dictionary divorced from the intrinsic evidence risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract, out of its particular context, which is the specification.

Phillips, 415 F.3d at 1321. By relying on non-technical dictionaries that have no connection to the '654 patent, Thermo has derived a construction that is technically inaccurate and contrary to a clear definition provided in the intrinsic record.[4]

As explained in Applera's opening brief, Applera's proposed construction arises from a definition of electroosmotic flow provided in the '382 patent. (D.I. 60 at 32). Thermo faults Applera for deriving its proposed construction from the '382 patent, because, according to Thermo, the '382 patent is only incorporated by reference for its disclosure of the operation of a thermal control for a particular capillary electrophoresis instrument. First, as explained above, the '654 patent incorporates the '382 patent in its entirety. *See supra* at 10. Accordingly, the '382 patent effectively becomes part of the specification '654 patent as if its text and drawings were physically contained therein. *Advanced Display*, 212 F.3d at 1282. It is, therefore, proper to look to '382 patent for guidance as to the meaning of "electroosmotic flow."

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[4] Thermo's reliance on its dictionary definitions is further flawed by its cherry-picking the words in the definitions that it wishes to include in its proposed construction. For example, both of its cited definitions discuss the movement of "liquid." (D.I. 57 at 28) (citing TA 6, 18). Yet, Thermo excludes the word "liquid" from its proposed construction, deliberately choosing instead to maintain its vague reference to "flow."

Even assuming, however, that the '654 patent does not incorporate the '382 patent's definition of "electroosmotic flow," it is still appropriate to look to the '382 patent in construing "electroosmotic flow" because it reflects what one of ordinary skill in the art would have understood "electroosmotic flow" to mean at the relevant time. Other contemporaneous references provide similar definitions. (*See* Grossman at 14, B 6 (defining "electroosmosis" as "the bulk flow of liquid due to the electric field on counterions adjacent to the negatively charged capillary wall.").

Thermo also incorrectly argues that Applera's construction is "inconsistent with the specification of the '654 patent" because it "imposes a limitation on the direction of the 'electroosmotic flow' by defining the flow in terms of the effect of an electric field on 'cations adjacent to anionic groups immobilized on the capillary wall.'" (D.I. 57 at 29). Thermo's argument evinces a misunderstanding of the '654 patent. As described in the '382 patent's definition of "electroosmotic flow," the capillary wall has a negative ("anionic") charge. Positively charged ions, *i.e.*, cations, therefore associate themselves with the negative charges on the capillary wall and a second layer of cations arranges itself just inside of the first layer. When an electrical field is applied, the inner layer of cations begins to move toward the cathode, pulling the fluid in the capillary along with it, resulting in "electroosmotic flow." The '382 patent provides this definition of electroosmotic flow and Applera adopts it: "the bulk flow of liquid due to the effect of an electric field on cations adjacent to anionic groups immobilized on the capillary wall."

Not only does the '382 patent define electroosmotic flow in this manner, but the '654 patent adopts the definition. The '654 patent describes the use of small cationic molecules as electroosmotic flow modifiers. Small cations bind to the negative charges

on the capillary wall, reducing or negating the negative charge. In such instances the cations in the carrier electrolyte do not associate themselves with the negatively charged wall, the cations are not pulled toward the cathode, and electroosmotic flow is thereby reduced or eliminated. In some instances, addition of an electroosmotic flow modifier renders the wall positively charged. In those instances, negatively charged ions associate themselves with the positive charges on the wall and, under the influence of an electric field, the anions migrate toward the anode, pulling the fluid in that direction and resulting in *reversed* electroosmotic flow. As highlighted by Thermo in its brief, the '654 patent describes electroosmotic flow and "reversed" electroosmotic flow in just this manner. (JA 15, 8:35-36 ("The addition of TTAB [cation] *reversed* the electroosmotic flow."); JA 14, 6:48-50 ("an electroosmotic flow modifier such as TTAB, which *reverses* the electroosmotic flow of the sample")) (emphasis added). The '654 patent adopts the definition of electroosmotic flow provided in the '382 patent by defining the reversal of electroosmotic flow as flow in the direction of the anode. Moreover, this understanding of reversing electroosmotic flow by providing ions to bind the capillary wall was understood by persons of skill in the art at the time the '654 patent application was filed. (*See* Grossman at 23, B 15 ("Using multivalent ions, one can even reverse the *direction* of the electroosmotic flow using this method.") (emphasis in original)). Applera's construction is consistent with the specification of '654 patent and accordingly should be adopted.

H. "Electroosmotic Flow Modifier"

Claim Term	Claim	Applera Proposal	Thermo Proposal
"electroosmotic flow modifier"	15	A small cationic molecule that neutralizes the charge on the capillary wall.	Substance that modifies the electroosmotic flow.

Thermo rests its construction of "electroosmotic flow modifier" on the '654 patent's general reference to there being "many electroosmotic flow modifiers known in the art." On the basis of this statement, Thermo alleges that claim 15 of the '654 patent covers *all* electroosmotic flow modifiers. That is a *non sequitur*. It does not follow from the existence of many known electroosmotic flow modifiers that the inventors meant to encompass all of them. (D.I. 57 at 29-30). Applera's construction embraces many electroosmotic flow modifiers, and thus is consistent with the manner that phrase is used in the specification.

The problem with Thermo's proposed construction is that it bears no relation to the invention the inventors described in the '654 patent. *See Wang Laboratories, Inc., v. America Online, Inc.,* 197 F.3d 1377, 1383 (Fed. Cir. 1999). Thermo's proposed "construction" of electroosmotic flow modifier is not really a construction at all but, instead is merely a shuffle of the words of the claim.

The electroosmotic flow modifiers identified in the '654 patent, diethylenetriamine ("DETA") and aliphatic trimethyl ammonium halides or hydroxides such as tetradecyltrimehlyammonium bromide ("TTAB"), are members of a well-known class of electroosmotic flow modifiers described in the contemporaneous literature as "small cationic molecules [that] neutralize the charge on the capillary wall." (Grossman at 23, B 15). The '654 patent describes no other class of electroosmotic flow modifiers or mechanism for inhibiting electroosmotic flow. Applera's construction adopts a

contemporaneous description of the class of electroosmotic flow modifiers that the patent actually describes for use in the invention.

According to Thermo, Applera's construction is wrong because it imposes a particular "polarity" on the electroosmotic flow modifier. Although Thermo does not make clear what it means by "polarity," Applera's construction is consistent with and arises directly from the definition of "electroosmotic flow" provided in the '382 patent and adopted in the '654 patent. As discussed above, "electroosmotic flow" is defined in the intrinsic record as the bulk flow of liquid due to the effect of an electric field on cations adjacent to anionic groups on a the capillary wall. Accordingly, the '654 patent discloses a group of cationic molecules that neutralize the negative charge on the capillary wall in order to "modify" or reverse the electroosmotic flow. Contrary to Thermo's contention, the '654 patent contains no mention of the use of "neutral" molecules, or any other type of molecule other than small cationic molecules, to modify electroosmotic flow.

Thermo's contention that Applera's construction improperly limits the scope of claim 15 is incorrect. Applera's construction explains the meaning of "electroosmotic flow modifier" in light of the invention described in the '654 patent specification, and it should, therefore, be adopted.

CONCLUSION

For the foregoing reasons, Applera respectfully requests that the Court adopt Applera's proposed constructions of the disputed terms of the '654 patent claims and reject Thermo's contrary constructions.

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CERTIFICATE OF SERVICE

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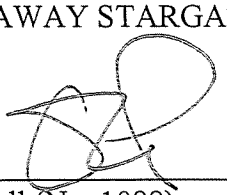

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